## REMARKS

Favorable reconsideration of this application as presently amended and in light of the following discussion is respectfully requested.

Claims 1-17 are pending in the present application. The present amendment cancels Claim 18 without prejudice or disclaimer; and amends Claims 1, 14 and 17 without introducing any new matter or raising new issues that would require further search and/or consideration.

In the outstanding Office Action, Claim 17 was objected to for informalities. Claim 18 was rejected under 35 U.S.C. § 112, first paragraph, as introducing new matter. Claims 1-18 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Claims 1-2, 8, and 11-12 were rejected under 35 U.S.C. § 102(e) as being anticipated by Lindsay et al. (U.S. Patent Publication No. 2004/0238379, hereinafter "Lindsay"). Claims 1-9 and 11-12 were rejected as unpatentable under 35 U.S.C. § 103(a) over the reference Lindsay in view of Kariyone et al. (U.S. Patent No. 5,242,793, hereinafter "Kariyone"). Claim 10 was rejected under 35 U.S.C. § 103(a) as unpatentable over the reference Lindsay in view of Kariyone, in further view of Hashimoto (U.S. Patent Publication No. 2001/0024788). Claim 13 was rejected as unpatentable under 35 U.S.C. § 103(a) over the reference Lindsay in view of Kariyone, in further view of Price (U.S. Patent No. 5,805,014). Claims 14-15 were rejected under 35 U.S.C. § 103(a) as unpatentable over the reference Lindsay in view of Kariyone, in further view of Hollis et al. (U.S. Patent No. 5,653,939, hereinafter "Hollis") and Dryja et al. (U.S. Patent No. 5,498,521, hereinafter "Dryja".) Claims 14 and 16 were rejected under 35 U.S.C. § 103(a) as unpatentable over the reference Lindsay in view of Kariyone, in further view of Hollis et al. (U.S. Patent No. 5,653,939, hereinafter "Hollis") and Sorenson (U.S. Patent No. 5,496,699).

In response, independent Claim 1 is amended to recite all the features of Applicants' dependent Claim 18. No new matter has been added. Consequently, dependent Claim 18 is cancelled without prejudice or disclaimer.

In response to the rejection of dependent Claim 18 under 35 U.S.C. § 112, first paragraph as introducing new matter, Applicants respectfully traverse this rejection and request reconsideration thereof, as next discussed.

Applicants respectfully submit that the gate electrode is clearly described in the disclosure as originally filed. As can be seen in Applicants' Fig. 1, and as clearly recited in Applicants' specification, the active region 3 between the source S and the drain D of the field effect transistor forms the gate region G, and a thin insulation layer 4 is provided on active region 3. (See also Specification, p. 5, ll. 23-31.) The measuring solution 6 covers the gate regions G, and the electrode E that is immerged in the electrolyte solution 6 fixes the potential of the electrolyte solution as well as the gate voltage of the transistors, to set the operation point of the sensors that include the transistors. (Specification, p. 7, ll. 10-20.) In particular, Applicants' specification recites that "[a]n electrode E ... is used to set the potential of the measuring solution 6 ... with respect to the silicon structure that it covers and to set the operating point of the sensors." (Specification, p. 7, ll. 10-14.) In addition, in Fig. 1 it can be seen that the voltage between electrode E and source S has been named $U_{GS}$ for a gate-source voltage.

In view of the above discussion, it is believed that the rejection of the features of Claim 18 under 35 U.S.C. § 112, first paragraph, is overcome.

In response to the objection to Claim 17 and the rejection of Claims 1 and 16 under 35 U.S.C. § 112, second paragraph, Claim 17 is amended to recite "at least one field-effect transistor." Moreover, Claim 1 is amended to recite that "at least two of the field-effect transistors having at least two active zones that are part of said some of active zones,

corresponding to a first group," and Claim 14 is amended to recite that the first and second enzymological reaction are performed in the first and second zones, respectively. In view of amended Claims 1 and 14, it is believed that all pending claims are definite and no further rejection on that basis is anticipated. If, however, the Examiner disagrees, the Examiner is invited to telephone the undersigned who will be happy to work with the Examiner in a joint effort to derive mutually acceptable language.

In response to the rejection of Claims 1-18 under 35 U.S.C. §§ 102(e) and 103(a), Applicants respectfully requests reconsideration of this rejection and traverse the rejection, as discussed next.

Briefly summarizing, Applicants' amended independent Claim 1 is directed to a method for detecting at least one parameter representative of molecular probes fixed to active zones of a sensor, wherein said sensor includes a network of field-effect transistors, each of which has a source region, a drain region, and a gate region which forms one of said active zones on which said representative parameter is detected. The method includes *inter alia* the steps of: bringing some of said active zones into contact with molecular probes in order to fix said probes; bathing at least said some of active zones which have been brought into contact with said molecular probes, in an electrolyte solution; measuring at least one point of at least one of a drain current, source-gate voltage, and source-drain voltage characteristic of at least two of the field-effect transistors, so as to deduce therefrom at least one said representative parameter ***by comparison between at least two measurements obtained for two different active zones*** immerged in said electrolyte solution, and ***fixing a potential of the electrolyte solution which covers said active zones with a gate electrode immerged in said electrolyte solution***.

The advantages of Applicants' independent Claim 1 in light of the specification are next discussed. By making comparative or differential measurements between conventional

FET transistors having a same gate voltage as well as the same voltage for the electrolyte solutions, the features of Applicants' Claim 1 allow making significant measurement improvements, by considerably increasing the sensitivity of a comparative or differential measurement. As explained in Applicants' specification at p. 7, ll. 10-20, with electrode F in the electrolyte solution, the voltage of the gates and of the electrolyte solution is no longer floating and is held at the same level, which avoids noise for a comparative or differential measure. Furthermore, as shown in Applicants' Fig. 8A-8C, the differential measurement shows current differences around 10 μA for drain current (Fig. 8A), or 150 mV for source-gate voltage (Fig. 8C), and about 60 mV for source gate voltage (Figs. 9C-9D). Please note that the above discussion is for explanatory purposes only, and is not intended to limit the scope of the claims in any fashion.

Turning now to the applied references, Lindsay is directed to a method for electronically detecting hybridization of a probe nucleic acid and a target nucleic acid. (Lindsay, Abstract.) For his method, Lindsay explains that a back-gated field effect transistor FET is used, where a layer of silicon 10 is provided on a buried oxide layer 20, located on a silicon wafer 30, where a source 40 and drain 50 and a n-channel 65 are provided in the silicon 10. (Lindsay, p. 2, ¶¶ [0019]-[0020], Fig. 1a.) A fluid placed on or in an upper surface 75 of n-cannel 65 the semiconductor can be charged to interact with the semiconductor. (Lindsay, p. 3, ¶ [0028], Figs. 1a, 1b). Lindsay also explains that when the FET is operated with a buffer including a DNA on the channel 65 for a measurement, an applied drain-source bias voltage 70 is kept constant, and a backgate voltage 60 $V_{bg}$ is grounded. (Lindsay, p. 4, ¶ [0036]-[0037], Fig. 7.) Consequently, in Lindsay the substrate is also grounded, as can be seen from Figs. 1a and 1b, indicating $V_{bg}$. Therefore, in the configuration shown in Lindsay, it is not possible that the potential of the buffer including the DNA and the gate is fixed, so that the same voltage is applied for all the transistors bathed by the buffer. Therefore,

Lindsay fails to teach fixing a potential of the electrolyte solution which covers said active zones with a gate electrode immerged in said electrolyte solution, as required by Applicants' amended Claim 1.

In addition, Applicants respectfully submit that Lindsay also fails to teach the comparing between at least two measurements obtained for two different active zones immerged in said electrolyte solution, as further recited in Applicants' independent Claim 1.

Lindsay mentions a differential measurement between the probe device output 210 and control output 220 and 200 along each thin oxide layer 110. (Lindsay, p. 3, ¶ [0032], Fig. 6.) But in Lindsay, as can be seen from Figure 6, the differential measurement is performed for ***the same*** thin oxide layer 110 of a FET. Therefore, Lindsay fails to teach comparing between at least two measurements obtained for ***two different active zones***, as required by Applicants' independent Claim 1.

To further support this position, Applicants are pointing to Lindsay's Fig. 7. In this figure, the evolution in the course of time of the source-drain current is shown, where curve 710 represents a 4pA change in the drain current when DNA is hybridized. (Lindsay, Fig. 7, ¶ [0033].) However, in Applicants' Fig. 6, current differences of 5-10$\mu$A are detected. Therefore, Lindsay's current level is extremely low and if a differential measurement were made from such small currents as required by Applicants' Claim 1, no result could be produced because noise from any differential amplifier or other sensing devices would be substantially higher than the differences measured.

The cited passages of the remaining references Kariyone, Hashimoto, Hollis, Dryja and/or Sorenson fail to remedy the deficiencies of Lindsay, even if we assume that any such combination is proper. In particular, these references fail to teach or suggest anything related to the comparing of two different measurements, and the fixing of the potential of the

electrolyte, as required by Applicants' Claim 1. Accordingly, Applicants respectfully traverse, and request reconsideration of this rejection based on these references.

The present amendment is submitted in accordance with the provisions of 37 C.F.R. § 1.116, which after Final Rejection permits entry of amendments complying with requirements of form set forth in a previous Office Action. As the present amendment merely amends independent Claim 1 to introduce the features of dependent Claim 18, and amends Claims 1, 14 and 17 to correct minor issues of form to overcome the objection and the rejection under 35 U.S.C. §§ 112, first and second paragraph, it is therefore respectfully requested that 37 C.F.R. § 1.116 be liberally construed, and that the present amendment be entered.

Consequently, in view of the present amendment, no further issues are believed to be outstanding in the present application, and the present application is believed to be in condition for formal Allowance. A Notice of Allowance for Claims 1-17 is earnestly solicited.

Should the Examiner deem that any further action is necessary to place this application in even better form for allowance, the Examiner is encouraged to contact Applicants' undersigned representative at the below listed telephone number.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.

N. Schibli

Gregory J. Maier
Attorney of Record
Registration No. 25,599

Nikolaus P. Schibli, Ph.D.
Registered Patent Agent
Registration No. 56,994

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 08/07)
RFF/rac

I:\ATTY\NPS\25'S\255977US\255977US-AM-OA.01.14.2008.DOC